CHEM 546: Classics in Total Synthesis — Spring 2015

Instructor: K.C. Nicolaou, BRC 363
kcn@rice.edu, 713-348-8860

Office Hours: Immediately after lectures or by appointment. There is a TA for this course.

Goals: This course is about the art and science of total synthesis of natural and designed molecules. Through select case studies, students learn several aspects of total synthesis, including the motivation for the synthesis, retrosynthetic analysis, synthetic strategy design, method development, chemical biology studies, and drug discovery and development. Emphasis is placed on both knowledge and creativity.

Prerequisites: CHEM 401 or 442

Required Texts:

1. K.C. Nicolaou and Jason Chen, *Classics in Total Synthesis III*, Wiley-VCH, **2011**. ISBN: 3-527-32957-9. Available from Wiley-VCH or Amazon (soft cover: $83.54; also available in Rice Bookstore).

Recommended Books:

1. K.C. Nicolaou and Scott Snyder, *Classics in Total Synthesis II*, Wiley-VCH, **2003**. ISBN: 3-527-30684-6. (Available in Rice Bookstore.)
2. K.C. Nicolaou and E.J. Sorensen, *Classics in Total Synthesis*, VCH, **1996**. ISBN: 3-527-29231-4.
3. K.C. Nicolaou and Tamsyn Montagnon, *Molecules That Changed the World*, Wiley-VCH, **2008**. ISBN: 3-527-29284-5.
4. László Kürti and Barbara Czakó, *Strategic Applications of Named Reactions in Organic Synthesis*, Academic Press, **2005**. ISBN: 978-0-12-429785-2.
5. E.J. Corey, László Kürti and Barbara Czakó, *Molecules and Medicine*, Wiley, **2007**. ISBN: 978-0-470-22749-7.
6. E.J. Corey and X. Cheng, *The Logic of Chemical Synthesis*, Wiley, **1989**. ISBN: 0-471-1159-0.
7. E.J. Corey and László Kürti, *Enantioselective Chemical Synthesis*, Direct Book Publishing, **2010**. ISBN: 978-0-615-39515-9.

Lectures and Tutorials: Lectures will be held in the BioScience Research Collaborative (BRC), Room 286, on Tuesdays and Thursdays from 9:25 – 10:40 a.m. Tutorials will be held in BRC, Room 308, from 7:00 – 8:00 p.m. on Tuesday nights.

Exams and Assignments: Exam: A comprehensive exam will be given on Thursday, February 26 during the normal class period. No make up exams will normally be allowed.

Assignment 1: Analysis of the total synthesis of a schindalactone A (*Angew. Chem. Int. Ed.* **2011**, *50*, 7373) in the classics style (5 pages total, including structures). Point out the innovative aspects of the work and the novel mechanisms of the key reactions involved.

Assignment 2: Proposal of a natural product total synthesis (3 pages, including schemes, excluding references). Target molecule must be cleared with instructor in advance. Emphasis should be placed on novel and imaginative synthetic strategies and modern methods.

Reading before each class: By doing so, you will be able to participate in class more effectively.

Grades:
Exam: 250 points
Assignment 1: 125 points
Assignment 2: 125 points

Disabilities: Student disabilities will be accommodated in accordance with the guidelines put forth by Disability Support Services (DSS). Students should register with the DSS Office in Allen Center and let the instructor know of their disabilities and needs as soon as possible.

Honor Code: The Rice University Honor Code applies to this course. Both assignments 1 and 2 are to be exclusively the work of each individual student. Proper references must be given to the original work when included in these home assignments.

Schedule
(Subject to Change)

Week 1	Tuesday, **Jan 13**	Lecture 1	Reserpine	Chapter 4, Classics I (handout will be given)
	Thursday, **Jan 15**	Lecture 2	Ginkgolide B	Chapter 25, Classics I (handout will be given)
Week 2	Tuesday, **Jan 20**	Lecture 3	Taxol	Chapter 34, Classics I (handout will be given)
	Thursday, **Jan 22**	Lecture 4	Tetrodotoxin	Chapter 2, Classics III
Week 3	Tuesday, **Jan 27**	Lecture 5	Littoralisone, Oseltamivir, Hirsutellone B	Chapter 7, Classics III
	Thursday, **Jan 29**	Lecture 6	Cyanthiwigns U & F	Chapter 9, Classics III
Week 4	Tuesday, **Feb 3**	Lecture 7	Sporolide B	Chapter 22, Classics III
	Thursday, **Feb 5**	Lecture 8	Lomaiviticin A	*J. Am. Chem. Soc.* **2011**, *133,* 7260 (reprint will be given)
Week 5	Tuesday, **Feb 10**	Lecture 9	Daphmanidin E	*Angew. Chem. Int. Ed.* **2011**, *50,* 11501 (reprint will be given)
	Thursday, **Feb 12**	Lecture 10	Acetylaranotin	*J. Am. Chem. Soc.* **2012**, *134,* 1930 (reprint will be given)
Week 6	Tuesday, **Feb 17**	Lecture 11	Viridicatumtoxin B	*Angew. Chem. Int. Ed.* **2013**, *52,* 8736 (reprint will be given)
	Thursday, **Feb 19**	Lecture 12	Ryanodol	*J. Am. Chem. Soc.* **2014**, *136,* 5916 (reprint will be given)
Week 7	Tuesday, **Feb 24**	Lecture 13	Taiwaniadducts B, C & D	*J. Am. Chem. Soc.* **2014**, *136,* 8185 (reprint will be given)
	Thursday, **Feb 26**	Exam		**Assignments 1 and 2 Due by Monday, March 2**